Mathematical epidemiology of the rubella epidemic in Japan (Theory of Biomathematics and Its Applications XII : Mathematical and experimental approach to clarify patterns in a transition process)

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Mathematical epidemiology of the rubella epidemic in Japan

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Introduction

A rubella epidemic occurred in Japan from 2012-14, involving more than 15,000 rubella cases, following with 45 notifications of congenital rubella syndrome (CRS). Symptoms of rubella tend to be mild and self-limiting, however, complications arises when pregnant women and the fetus are infected, especially during the first trimester of pregnancy. Rubella vaccination in Japan was introduced in 1976, initially only targeting females for individual protection towards CRS, later in 1995, the policy shifted to target both genders to elevate and maintain herd immunity. The present study aimed to evaluate the past vaccination program in Japan, by characterizing the features which led to experience the 2012-14 epidemic, with the analysis of the age-dependent transmission dynamics, to explicitly assess how the herd immunity is achieved, and how pregnant women have been protected over time.

Methods

Time series of incidence and serological data from 1983-2014 was used for assessing male and female immune status against rubella. The herd immunity threshold $1-1/(R_0)$, was calculated 83.6%, from the R_0 estimated 6.1 for rubella [1], as an index whether major epidemic will be prevented. Susceptible pockets were analyzed with the age-specific proportion seropositive, and birth year cohort. The median, and interquartile of age at infection was calculated.

Two evaluation metrics were applied to assess herd immunity at the population level. First, we calculated the age-standardized seroprevalence, $m_{1,g}(t)$, at calendar time t and in gender g ($g = 0$ for female or 1 for male), as

$$m_{1,g}(t) = \sum_{a=0}^{\infty} \left(1 - p_{a,g}(t)\right) n_{a,g}(t),$$

where $p_{a,g}(t)$ is the observed seropositive proportion and $n_{a,g}(t)$ is the relative population size at time t and gender g in age group a. This metric is interpreted as the age-standardized seronegative proportion.

Secondly, to assess the risk of CRS over time, the absolute number of live births at risk of developing CRS was calculated at time t using the age-specific annual number of live births, $b_a(t)$, and the age-specific seronegative proportion in the corresponding age-group:

$$m_2(t) = \sum_{a=a_L}^{a_U} \left(1 - p_{a,0}(t)\right) b_a(t),$$

where a_L and a_U represent the lower and upper childbearing ages of mothers, respectively. The childbearing age was assumed to be 0 to 49. The 95% confidence intervals were derived from the normal approximation to the binomial distribution in both metrics.

Results

Susceptible pockets were identified in the male birth cohorts of 1973-78 and 1989-93 with the lowest proportion seropositive of 68.0% and 70.0%. A minor pocket was observable in the female birth cohort of 1989-93 with proportion seropositive of 78.3%. From 1982-2014, there was an increase of age at infection both among male and female (p=<o.ool). Age-standardized proportion seronegative steadily dropped from 1983, 46.8% (CI 18.2-75.4%) and 33.3% (CI 29.4-37.2%) among male and female, to 18.6% (CI 17.0-20.0%) and 15.6% (CI 10.1-21.1%), respectively in 2013 (Figure A). Susceptible live births were reduced from 1983 calculated 172,885 cases to 23,893 cases in 2013 (Figure B).

Discussion

As an important background to have driven the 2012-14 epidemic, susceptible pockets were identified especially among adult male cohorts. Making rubella control more difficult, there has been an increase in the age at infection. Although the absolute number of rubella cases has been decreasing over time, the occurrence of the epidemic was fueled by the insufficient herd immunity, and thus, the tragedy that was identified in Greece in the 1990s [2]

was repeatedly experienced.

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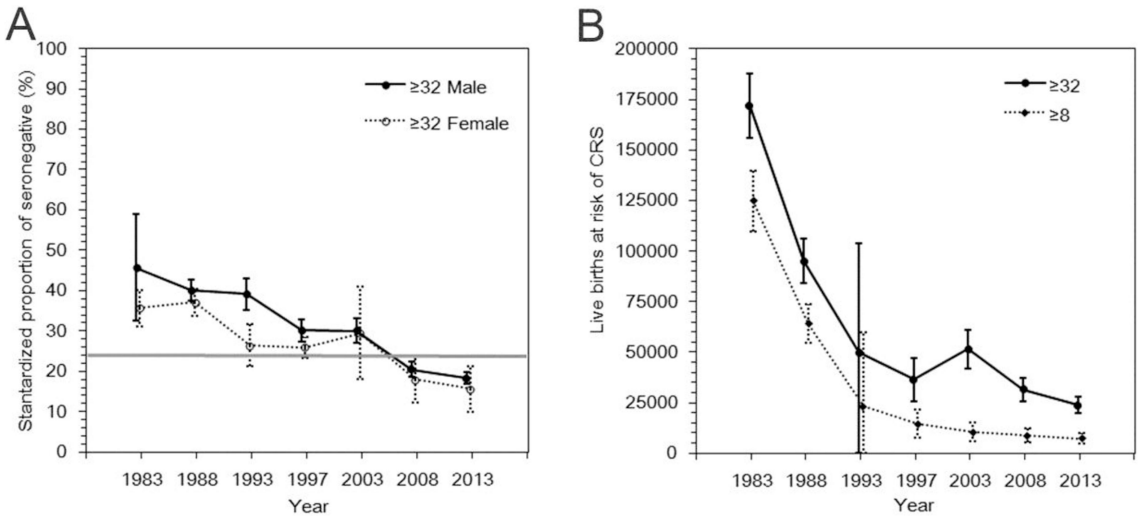

Figure. Time-dependence in the standardized rubella-seronegative proportion (Figure A) and the number of live births at risk for CRS in Japan, 1983–2013 (Figure B).

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